WHAT IS CLAIMED:

1. A method for identifying one or more of a plurality of sequences differing by one or more single-base changes, insertions, deletions, or translocations in a plurality of target nucleotide sequences comprising:

providing a sample potentially containing one or more target nucleotide sequences with a plurality of sequence differences;

providing a plurality of oligonucleotide probe sets, each set characterized by (a) a first oligonucleotide probe, having a target-specific portion and an addressable array-specific portion, and (b) a second oligonucleotide probe, having a target-specific portion and a detectable reporter label, wherein the oligonucleotide probes in a particular set are suitable for ligation together when hybridized adjacent to one another on a corresponding target nucleotide sequence, but have a mismatch which interferes with such ligation when hybridized to any other nucleotide sequence present in the sample;

providing a ligase,

blending the sample, the plurality of oligonucleotide probe sets, and the ligase to form a mixture;

subjecting the mixture to one or more ligase detection reaction cycles comprising a denaturation treatment, wherein any hybridized oligonucleotides are separated from the target nucleotide sequences, and a hybridization treatment, wherein the oligonucleotide probe sets hybridize at adjacent positions in a base-specific manner to their respective target nucleotide sequences, if present in the sample, and ligate to one another to form a ligated product sequence containing (a) the addressable array-specific portion, (b) the target-specific portions connected together, and (c) the detectable reporter label, and, wherein the oligonucleotide probe sets may hybridize to nucleotide sequences in the sample other than their respective target nucleotide sequences but do not ligate together due to a presence of one or more mismatches and individually separate during the denaturation treatment;

providing a solid support with different capture oligonucleotides immobilized at particular sites, wherein the capture oligonucleotides have nucleotide sequences complementary to the addressable array-specific portions;

contacting the mixture, after said subjecting, with the solid support under conditions effective to hybridize the addressable array-specific portions to the capture oligonucleotides in a base-specific manner, thereby capturing the addressable array-specific portions on the solid support at the site with the complementary capture oligonucleotide; and

detecting the reporter labels of ligated product sequences captured to the solid support at particular sites, thereby indicating the presence of one or more target nucleotide sequences in the sample.

2. A method according to claim 1, wherein the oligonucleotide probes in a set are suitable for ligation together at a ligation junction when hybridized adjacent to one

another on a corresponding target nucleotide sequence due to perfect complementarity at the ligation junction, but, when the oligonucleotide probes in the set are hybridized to any other nucleotide sequence present in the sample, have a mismatch at a base at the ligation junction which interferes with such ligation.

3. A method according to claim 2, wherein the mismatch is at the 3' base at the ligation junction.

4. A method according to claim 1, wherein the oligonucleotide probes in a set are suitable for ligation together at a ligation junction when hybridized adjacent to one another on a corresponding target nucleotide sequence due to perfect complementarity at the ligation junction, but, when the oligonucleotide probes in the set are hybridized to any other nucleotide sequence present in the sample, there is a mismatch at a base adjacent to a base at the ligation junction which interferes with such ligation.

5. A method according to claim 4, wherein the mismatch is at the base adjacent to the 3' base at the ligation junction.

6. A method according to claim 1, wherein the sample potentially contains unknown amounts of one or more of a plurality of target sequences with a plurality of sequence differences, said method further comprising:

quantifying, after said detecting, the amount of the target nucleotide sequences in the sample by comparing the amount of captured ligated product sequences generated from the sample with a calibration curve of captured ligated product sequences generated from samples with known amounts of the target nucleotide sequence.

7. A method according to claim 1, wherein the sample potentially contains unknown amounts of one or more of a plurality of target nucleotide sequences with a plurality of sequence differences, said method further comprising:

providing a known amount of one or more marker target nucleotide sequences;

providing a plurality of marker-specific oligonucleotide probe sets, each set characterized by (a) a first oligonucleotide probe, having a target-specific portion complementary to the marker target nucleotide sequence and an addressable array-specific portion complementary to capture oligonucleotides on the solid support, and (b) a second oligonucleotide probe, having a target-specific portion complementary to the marker target nucleotide sequence and a detectable reporter label, wherein the oligonucleotide probes in a particular marker-specific oligonucleotide set are suitable for ligation together when hybridized adjacent to one another on a corresponding marker target nucleotide sequence, but, when hybridized to any other nucleotide sequence present in the sample or added

marker sequences, there is a mismatch which interferes with such ligation, wherein said blending comprises blending the sample, the marker target nucleotide sequences, the plurality of oligonucleotide probe sets, the plurality of marker-specific oligonucleotide probe sets, and the ligase to form a mixture;

detecting the reporter labels of the ligated marker-specific oligonucleotide sets captured on the solid support at particular sites, thereby indicating the presence of one or more marker target nucleotide sequences in the sample; and

quantifying the amount of target nucleotide sequences in the sample by comparing the amount of captured ligated product generated from the known amount of marker target nucleotide sequences with the amount of captured other ligated product.

8. A method according to claim 7, wherein the one or more marker target nucleotide sequences differ from the target nucleotide sequences in the sample at one or more single nucleotide positions.

9. A method according to claim 8, wherein the oligonucleotide probe sets and the marker-specific oligonucleotide probe sets form a plurality of oligonucleotide probe groups, each group comprised of one or more oligonucleotide probe sets designed for distinguishing multiple allele differences at a single nucleotide position, wherein, in the oligonucleotide probe sets of each group, the first oligonucleotide probes have a common target-specific portion, and the second oligonucleotide probes have a differing target-specific portion which hybridize to a given allele or a marker nucleotide sequence in a base-specific manner.

10. A method according to claim 8, wherein the oligonucleotide probe sets and the marker-specific oligonucleotide probe sets form a plurality of oligonucleotide probe groups, each group comprised of one or more oligonucleotide probe sets designed for distinguishing multiple allele differences at a single nucleotide position, wherein, in the oligonucleotide probe sets of each group, the second oligonucleotide probes have a common target-specific portion and the first oligonucleotide probe have differing target-specific portions, which hybridize to a given allele or a marker nucleotide sequence in a base-specific manner.

11. A method according to claim 1, wherein the sample potentially contains unknown amounts of two or more of a plurality of target nucleotide sequences with a plurality of sequence differences, said method further comprising:

quantifying, after said detecting, the relative amount of each of the plurality of target nucleotide sequences in the sample by comparing the relative amount of captured ligated product sequences generated by each of the plurality of target sequences within the

sample, thereby providing a quantitative measure of the relative level of two or more target nucleotide sequences in the sample.

12. A method according to claim 1, wherein multiple allele differences at two or more nearby or adjacent nucleotide positions in a single target nucleotide sequence or multiple allele differences at two or more nearby or adjacent nucleotide positions in multiple target nucleotide sequences are distinguished with oligonucleotide probe sets having oligonucleotide probes with target-specific portions which overlap.

13. A method according to claim 1, wherein the target-specific portions of the oligonucleotide probe sets have substantially the same melting temperature so that they hybridize to target nucleotide sequences under similar hybridization conditions.

14. A method according to claim 1, wherein multiple allele differences at one or more nucleotide position in a single target nucleotide sequence or multiple allele differences at one or more positions in multiple target nucleotide sequences are distinguished, the oligonucleotide probe sets forming a plurality of oligonucleotide probe groups, each group comprised of one or more oligonucleotide probe sets designed for distinguishing multiple allele differences at a single nucleotide position, wherein, in the oligonucleotide probes of each group, the second oligonucleotide probes have a common target-specific portion and the first oligonucleotide probes have differing target-specific portions which hybridize to a given allele in a base-specific manner, wherein, in said detecting, the labels of ligated product sequences of each group, captured on the solid support at different sites, are detected, thereby indicating a presence, in the sample of one or more allele at one or more nucleotide position in one or more target nucleotide sequences.

15. A method according to claim 14, wherein the oligonucleotide probes in a given set are suitable for ligation together at a ligation junction when hybridized adjacent to one another on a corresponding target nucleotide sequence due to perfect complementarity at the ligation junction, but, when hybridized to any other nucleotide sequence present in the sample, the first oligonucleotide probe has a mismatch at a base at the ligation junction which interferes with such ligation.

16. A method according to claim 14, wherein multiple allele differences at two or more nearby or adjacent nucleotide positions in a single target nucleotide sequence or multiple allele differences at two or more nearby or adjacent nucleotide positions in multiple target nucleotide sequences are distinguished with oligonucleotide probe groups having oligonucleotide probes with target-specific portions which overlap.

17. A method according to claim 16, wherein the oligonucleotide probes in a set are suitable for ligation together at a ligation junction when hybridized adjacent to one another on a corresponding target nucleotide sequence due to perfect complementarity at the ligation junction, but, when the oligonucleotide probes in the set are hybridized to any other nucleotide sequence present in the sample, there is a mismatch at a base at the ligation junction which interferes with such ligation .

18. A method according to claim 1, wherein multiple allele differences consisting of insertions, deletions, microsatellite repeats, translocations, or other DNA rearrangements at one or more nearby positions in a single target nucleotide sequence or multiple allele differences consisting of insertions, deletions, microsatellite repeats, translocations, or other DNA rearrangements at one or more nearby positions in multiple target nucleotide sequences are distinguished, the oligonucleotide probe sets forming a plurality of oligonucleotide probe groups, each group comprised of one or more oligonucleotide probe sets designed for distinguishing multiple allele differences selected from the group consisting of insertions, deletions, microsatellite repeats, translocations, and other DNA rearrangements at one or more nearby positions, wherein, in the oligonucleotide probe sets of each group, the second oligonucleotide probes have a common target-specific portion and the first oligonucleotide probes have differing target-specific portions which hybridize to a given allele in a base-specific manner, wherein, in said detecting, the labels of ligated product sequences of each group, captured on the solid support at different sites, are detected, thereby indicating a presence, in the sample, of one or more allele differences selected from the group consisting of insertions, deletions, microsatellite repeats, translocations, and other DNA rearrangements in one or more target nucleotide sequences.

19. A method according to claim 18, wherein the oligonucleotide probe sets are designed for distinguishing multiple allele differences selected from the group consisting of insertions, deletions, and microsatellite repeats, at one or more nearby positions, wherein, in the oligonucleotide probe sets of each group, the second oligonucleotide probes have a common target-specific portion, and the first oligonucleotide probes have differing target-specific portions which contain repetitive sequences of different lengths to hybridize to a given allele in a base-specific manner.

20. A method according to claim 1, wherein a low abundance of multiple allele differences at multiple nearby or adjacent positions in a single target nucleotide sequence, in the presence of an excess of normal sequence, or a low abundance of multiple allele differences at multiple nearby positions in multiple target nucleotide sequences, in the presence of an excess of normal sequence, are distinguished, the oligonucleotide probe sets forming a plurality of oligonucleotide probe groups, each group comprised of one or

more oligonucleotide probe sets designed for distinguishing multiple allele differences at a single nucleotide position, wherein one or more sets within a group share common second oligonucleotide probes and the first oligonucleotide probes have differing target-specific portions which hybridize to a given allele excluding the normal allele in a base-specific manner, wherein, in said detecting, the labels of ligated product sequences of each group captured on the solid support at different sites, are detected, thereby indicating a presence, in the sample, of one or more low abundance alleles at one or more nucleotide positions in one or more target nucleotide sequences.

21. A method according to claim 20, wherein the oligonucleotide probes in a set are suitable for ligation together at a ligation junction when hybridized adjacent to one another on a corresponding target nucleotide sequence due to perfect complementarity at the ligation junction, but, when the oligonucleotide probes in the set are hybridized to any other nucleotide sequence present in the sample, the first oligonucleotide probes have a mismatch at a base at the ligation junction which interferes with such ligation.

22. A method according to claim 20, wherein a low abundance of multiple allele differences at multiple nearby or adjacent positions in a single target nucleotide sequence, in the presence of an excess of normal sequence, or a low abundance of multiple allele differences at multiple nearby positions in multiple target nucleotide sequences, in the presence of an excess of normal sequence, are quantified in a sample, said method further comprising:

providing a known amount of one or more marker target nucleotide sequences;

providing a plurality of marker-specific oligonucleotide probe sets, each set characterized by (a) a first oligonucleotide probe having a target-specific portion complementary to the marker target nucleotide sequence and an addressable array-specific portion, and (b) a second oligonucleotide probe, having a target-specific portion complementary to the marker target nucleotide sequence and a detectable reporter label, wherein the oligonucleotide probes in a particular marker-specific oligonucleotide set are suitable for ligation together when hybridized adjacent to one another on a corresponding marker target nucleotide sequence, but, when hybridized to any other nucleotide sequence present in the sample or added marker sequences, have a mismatch which interferes with such ligation;

providing a plurality of oligonucleotide probe groups, each group comprised of one or more oligonucleotide probe sets or marker-specific oligonucleotide probe sets designed for distinguishing multiple allele differences at a single nucleotide position, including marker nucleotide sequences, wherein one or more sets within a group share a common second oligonucleotide probe and the first oligonucleotide probes have different target-specific probe portions which hybridize to a given allele or a marker

nucleotide sequence excluding the normal allele, in a base-specific manner, wherein said blending comprises blending the sample, the marker target nucleotide sequences, the plurality of oligonucleotide probe sets, the plurality of marker-specific oligonucleotide probe sets, and the ligase to form a mixture;

detecting the reporter labels of the ligated marker-specific oligonucleotide sets captured on the solid support at particular sites, thereby indicating the presence of one or more marker target nucleotide sequences in the sample; and

quantifying the amount of target nucleotide sequences in the sample by comparing the amount of captured ligated products generated from the known amount of marker target nucleotide sequences with the amount of other captured ligated product generated from the low abundance unknown sample.

23. A method according to claim 22, wherein the oligonucleotide probes in a set are suitable for ligation together at a ligation junction when hybridized adjacent to one another on a corresponding target nucleotide sequence under selected conditions due to perfect complementarity at the ligation junction, but, when the oligonucleotide probes in the set are hybridized to any other nucleotide sequence present in the sample, the first oligonucleotide probes have a mismatch at a base at the ligation junction which interferes with such ligation.

24. A method according to claim 1, wherein multiple allele differences at one or more nucleotide position in a single target nucleotide sequence or multiple allele differences at one or more positions in multiple target nucleotide sequences are distinguished, the oligonucleotide sets forming a plurality of oligonucleotide probe groups, each group comprised of one or more oligonucleotide probe sets designed for distinguishing multiple allele differences at a single nucleotide position, wherein, in the oligonucleotide probes of each group, the first oligonucleotide probes have a common target-specific portion and the second oligonucleotide probes have differing target-specific portions which hybridize to a given allele in a base-specific manner, wherein, in said detecting, different reporter labels of ligated product sequences of each group captured on the solid support at particular sites are detected, thereby indicating a presence, in the sample, of one or more allele at one or more nucleotide positions in one or more target nucleotide sequences.

25. A method according to claim 24, wherein the oligonucleotide probes in a set are suitable for ligation together at a ligation junction when hybridized adjacent to one another on a corresponding target nucleotide sequence due to perfect complementarity at the ligation junction, but, when the oligonucleotide probes in the set are hybridized to any other nucleotide sequence present in the sample, the second oligonucleotide probes have a mismatch at a base at the ligation junction which interferes with such ligation.

26. A method according to claim 24, wherein multiple allele differences at two or more nearby or adjacent nucleotide positions in a single target nucleotide sequence, or multiple allele differences at two or more nearby or adjacent nucleotide positions in multiple target nucleotide sequences are distinguished, the oligonucleotide probe groups containing oligonucleotide probes with target-specific portions which overlap.

27. A method according to claim 26, wherein the oligonucleotide probes in a set are suitable for ligation together at a ligation junction when hybridized adjacent to one another on a corresponding target nucleotide sequence due to perfect complementarity at the ligation junction, but, when the oligonucleotide probes in the set are hybridized to any other nucleotide sequence present in the sample, the second oligonucleotide probe has a mismatch at a base at the ligation junction which interferes with such ligation.

28. A method according to claim 1, wherein multiple allele differences at one or more nucleotide position in a single target nucleotide sequence or multiple allele differences at one or more positions in multiple target nucleotide sequences are distinguished, the oligonucleotide sets forming a plurality of probe groups, each group comprised of one or more oligonucleotide probe sets designed for distinguishing multiple allele differences at a single nucleotide position, wherein, in the oligonucleotide probes of different groups, the second oligonucleotide probes have a common target-specific portion or the first oligonucleotide probes have a common target-specific portion, wherein, in said detecting, the one of a plurality of labeled ligated product sequences of each group captured on the solid support at particular sites are detected, thereby indicating a presence of one or more allele at one or more nucleotide positions in one or more target nucleotide sequences in the sample.

29. A method according to claim 28, wherein the oligonucleotide probes in a given set are suitable for ligation together at ligation junction when hybridized adjacent to one another on a corresponding target nucleotide sequence due to perfect complementarity at the ligation junction but, when the oligonucleotides in the set are hybridized to any other nucleotide sequence present in the sample, the first or second oligonucleotide probes have a mismatch at a base at the ligation junction which interferes with such ligation.

30. A method according to claim 28, wherein multiple allele differences at two or more nearby or adjacent nucleotide positions in a target nucleotide sequence or multiple allele differences at two or more nearby or adjacent nucleotide positions in multiple target nucleotide sequence are distinguished, the oligonucleotide probe groups containing probes with target-specific portions which overlap.

31. A method according to claim 30, wherein oligonucleotide probes in a set are suitable for ligation together at a ligation junction when hybridized adjacent to one another on a corresponding target nucleotide sequence due to perfect complementarity at the ligation junction, but, when the oligonucleotides in the set are hybridized to any other nucleotide sequence present in the sample, the first or second oligonucleotide probes have a mismatch at a base at the ligation junction which interferes with such ligation.

32. A method according to claim 29, wherein all possible single-base mutations for a single codon in a single target nucleotide sequence, all possible single-base mutations for multiple codons in a single target nucleotide sequence, and all possible single-base mutations for multiple codons in multiple target nucleotide sequences are distinguished, the oligonucleotide sets forming a plurality of oligonucleotide probe groups, each group comprised of one or more oligonucleotide probe sets designed for distinguishing all possible single-base mutations for a single codon, wherein, in the oligonucleotide probes of each group, the second oligonucleotide probes differ only in their 5' bases at their ligation junction and contain different reporter labels, the first oligonucleotide probes differ only in their 3' bases at their ligation junction and contain different addressable array-specific portions, or the first oligonucleotide probes differ only in their 3' bases adjacent to the base at the ligation junction and contain different addressable array-specific portions.

33. A method according to claim 29, wherein the oligonucleotide probes in a set are suitable for ligation together at a ligation junction when hybridized adjacent to one another on a corresponding target nucleotide sequence due to perfect complementarity at the ligation junction, but, when the oligonucleotides in the set are hybridized to any other nucleotide sequence present in the sample, the first oligonucleotide probes have a mismatch at the 3' base at the ligation junction or the 3' base adjacent the base at the ligation junction or the second oligonucleotide probes have a mismatch at the 5' base at the ligation junction which interferes with such ligation.

34. A method according to claim 33, wherein all possible single-base mutations for a single codon in a single target nucleotide sequence, or all possible single-base mutations for two or more nearby or adjacent codons in multiple target nucleotide sequences are distinguished, the oligonucleotide probe groups containing oligonucleotide probes with target-specific portions which overlap.

35. A method according to claim 1, wherein the denaturation treatment is at a temperature of about 80°-105°C.

36. A method according to claim 1, wherein each cycle, comprising a denaturation treatment and a hybridization treatment, is from about 30 seconds to about five minutes long.

37. A method according to claim 1, wherein said subjecting is repeated for 2 to 50 cycles.

38. A method according to claim 1, wherein total time for said subjecting is 1 to 250 minutes.

39. A method according to claim 1, wherein the ligase is selected from the group consisting of *Thermus aquaticus* ligase, *Thermus thermophilus* ligase, *E. coli* ligase, T4 ligase, and *Pyrococcus* ligase.

40. A method according to claim 1, wherein the detectable reporter label is selected from the group consisting of chromophores, fluorescent moieties, enzymes, antigens, heavy metals, magnetic probes, dyes, phosphorescent groups, radioactive materials, chemiluminescent moieties, and electrochemical detecting moieties.

41. A method according to claim 1, wherein the target-specific portions of the oligonucleotide probes each have a hybridization temperature of 20-85°C.

42. A method according to claim 1, wherein the target-specific portions of the oligonucleotide probes are 20 to 28 nucleotides long.

43. A method according to claim 1, wherein the mixture further includes a carrier DNA.

44. A method according to claim 1, wherein said subjecting achieves a rate of formation of mismatched ligated product sequences which is less than .005 of the rate of formation of matched ligated product sequences.

45. A method according to claim 1 further comprising:
amplifying the target nucleotide sequences in the sample prior to said blending.

46. A method according to claim 45, wherein said amplifying is carried out by subjecting the sample to a polymerase-based amplifying procedure.

47. A method according to claim 45, wherein said polymerase-based amplifying procedure is carried out with DNA polymerase.

48. A method according to claim 45, wherein said polymerase-based amplifying procedure is carried out with reverse transcriptase.

49. A method according to claim 45, wherein said polymerase-based amplifying procedure is carried out with RNA polymerase.

50. A method according to claim 45, wherein said amplifying is carried out by subjecting the target nucleotide sequences in the sample to a ligase chain reaction process.

51. A method according to claim 1, wherein the oligonucleotide probe sets are selected from the group consisting of ribonucleotides, deoxyribonucleotides, modified ribonucleotides, modified deoxyribonucleotides, peptide nucleic acids, modified peptide nucleic acids, modified phosphate-sugar backbone oligonucleotides, nucleotide analogues, and mixtures thereof.

52. A method according to claim 1, wherein said method is used to detect infectious diseases caused by bacterial, viral, parasitic, and fungal infectious agents.

53. A method according to claim 52, wherein the infectious disease is caused by a bacteria selected from the group consisting of *Escherichia coli, Salmonella, Shigella, Klebsiella, Pseudomonas, Listeria monocytogenes, Mycobacterium tuberculosis, Mycobacterium avium-intracellulare, Yersinia, Francisella, Pasteurella, Brucella, Clostridia, Bordetella pertussis,* Bacteroides, *Staphylococcus aureus, Streptococcus pneumonia,* B-Hemolytic strep., *Corynebacteria, Legionella, Mycoplasma, Ureaplasma, Chlamydia, Neisseria gonorrhea, Neisseria meningitides, Hemophilus influenza, Enterococcus faecalis, Proteus vulgaris, Proteus mirabilis, Helicobacter pylori, Treponema palladium, Borrelia burgdorferi, Borrelia recurrentis, Rickettsial* pathogens, *Nocardia,* and *Acitnomycetes.*

54. A method according to claim 52, wherein the infectious disease is caused by a fungal infectious agent selected from the group consisting of *Cryptococcus neoformans, Blastomyces dermatitidis, Histoplasma capsulatum, Coccidioides immitis, Paracoccicioides brasiliensis, Candida albicans, Aspergillus fumigautus, Phycomycetes (Rhizopus), Sporothrix schenckii, Chromomycosis,* and *Maduromycosis.*

55. A method according to claim 52, wherein the infectious disease is caused by a viral infectious agent selected from the group consisting of human immunodeficiency

virus, human T-cell lymphocytotrophic viurs, hepatitis viruses (e.g., Hepatitis B Virus and Hepatitis C Virus), Epstein-Barr Virus, cytomegalovirus, human papillomaviruses, orthomyxo viruses, paramyxo viruses, adenoviruses, corona viruses, rhabdo viruses, polio viruses, toga viruses, bunya viruses, arena viruses, rubella viruses, and reo viruses.

56. A method according to claim 52, wherein the infectious disease is caused by a parasitic infectious agent selected from the group consisting of *Plasmodium falciparum, Plasmodium malaria, Plasmodium vivax, Plasmodium ovale, Onchoverva volvulus, Leishmania, Trypanosoma* spp., *Schistosoma* spp., *Entamoeba histolytica, Cryptosporidum, Giardia* spp., *Trichimonas* spp., *Balatidium coli, Wuchereria bancrofti, Toxoplasma* spp., *Enterobius vermicularis, Ascaris lumbricoides, Trichuris trichiura, Dracunculus medinesis,* trematodes, *Diphyllobothrium latum, Taenia* spp., *Pneumocystis carinii,* and *Necator americanis.*

57. A method according to claim 1, wherein said method is used to detect genetic diseases.

58. A method according to claim 57, wherein the genetic disease is selected from the group consisting of 21 hydroxylase deficiency, cystic fibrosis, Fragile X Syndrome, Turner Syndrome, Duchenne Muscular Dystrophy, Down Syndrome, heart disease, single gene diseases, HLA typing, phenylketonuria, sickle cell anemia, Tay-Sachs Syndrome, thalassemia, Klinefelter's Syndrome, Huntington's Disease, autoimmune diseases, lipidosis, obesity defects, hemophilia, inborn errors in metabolism, and diabetes.

59. A method according to claim 1, wherein said method is used to detect cancer involving oncogenes, tumor suppressor genes, or genes involved in DNA amplification, replication, recombination, or repair.

60. A method according to claim 59, wherein the cancer is associated with a gene selected from the group consisting of BRCA1 gene, p53 gene, *Familial polyposis coli*, Her2/Neu amplification, Bcr/Ab1, K-ras gene, human papillomavirus Types 16 and 18, leukemia, colon cancer, breast cancer, lung cancer, prostate cancer, brain tumors, central nervous system tumors, bladder tumors, melanomas, liver cancer, osteosarcoma and other bone cancers, testicular and ovarian carcinomas, ENT tumors, and loss of heterozygosity.

61. A method according to claim 1, wherein said method is used for environmental monitoring, forensics, and food and feed industry monitoring.

62. A method according to claim 1, wherein the solid support is made from a material selected from the group consisting of plastic, ceramic, metal, resin, gel, glass, silicon, and composites thereof.

63. A method according to claim 1, wherein the solid support is in a form selected from the group consisting of slides, discs, membranes, films, and composites thereof.

64. A method according to claim 1, wherein the solid support has an array of positions with the capture oligonucleotides attached to positions in the array.

65. A method according to claim 64, wherein the solid support has wells, raised regions, or etched trenches.

66. A method according to claim 64, wherein the solid support is in the form of a microtiter plate.

67. A method according to claim 1, wherein the solid support is functionalized with olefin, amino, hydroxyl, silanol, aldehyde, keto, halo, acyl halide, or carboxyl groups.

68. A method according to claim 67, wherein the solid support is functionalized with an amino group by reaction with an amine compound selected from the group consisting of 3-aminopropyl triethoxysilane, 3-aminopropylmethyldiethoxysilane, 3-aminopropyl dimethylethoxysilane, 3-aminopropyl trimethoxysilane, N-(2-aminoethyl)-3-aminopropylmethyl dimethoxysilane, N-(2-aminoethyl-3-aminopropyl) trimethoxysilane, aminophenyl trimethoxysilane, 4-aminobutyldimethyl methoxysilane, 4-aminobutyl triethoxysilane, aminoethylaminomethylphenethyl trimethoxysilane, and mixtures thereof.

69. A method according to claim 67, wherein the solid support is functionalized with an olefin-containing silane.

70. A method according to claim 69, wherein the olefin-containing silane is selected from the group consisting of 3-(trimethoxysilyl)propyl methacrylate, *N*-[3-(trimethoxysilyl)propyl]-*N'*-(4-vinylbenzyl)ethylenediamine, triethoxyvinylsilane, triethylvinylsilane, vinyltrichlorosilane, vinyltrimethoxysilane, vinyltrimethylsilane, and mixtures thereof.

71. A method according to claim 69 wherein the silanized support is polymerized with an olefin containing monomer.

72. A method according to claim 71, wherein the olefin-containing monomer contains a functional group.

73. A method according to claim 72, wherein the the olefin-containing monomer is selected from the group consisting of acrylic acid, methacrylic acid, vinylacetic acid, 4-vinylbenzoic acid, itaconic acid, allyl amine, allylethylamine, 4-aminostyrene, 2-aminoethyl methacrylate, acryloyl chloride, methacryloyl chloride, chlorostyrene, dichlorostyrene, 4-hydroxystyrene, hydroxymethylstyrene, vinylbenzyl alcohol, allyl alcohol, 2-hydroxyethyl methacrylate, poly(ethylene glycol) methacrylate, and mixtures thereof.

74. A method according to claim 71, wherein the support is polymerized with a monomer selected from the group consisting of acrylic acid, methacrylic acid, vinylacetic acid, 4-vinylbenzoic acid, itaconic acid, allyl amine, allylethylamine, 4-aminostyrene, 2-aminoethyl methacrylate, acryloyl chloride, methacryloyl chloride, chlorostyrene, dischlorostyrene, 4-hydroxystyrene, hydroxymethyl styrene, vinylbenzyl alcohol, allyl alcohol, 2-hydroxyethyl methacrylate, poly(ethylene glycol) methacrylate, and mixtures thereof, together with a monomer selected from the group consisting of acrylic acid, acrylamide, methacrylic acid, vinylacetic acid, 4-vinylbenzoic acid, itaconic acid, allyl amine, allylethylamine, 4-aminostyrene, 2-aminoethyl methacrylate, acryloyl chloride, methacryloyl chloride, chlorostyrene, dichlorostyrene, 4-hydroxystyrene, hydroxymethyl styrene, vinylbenzyl alcohol, allyl alcohol, 2-hydroxyethyl methacrylate, poly(ethylene glycol) methacrylate, methyl acrylate, methyl methacrylate, ethyl acrylate, ethyl methacrylate, styrene, 1-vinylimidazole, 2-vinylpyridine, 4-vinylpyridine, divinylbenzene, ethylene glycol dimethacrylate, *N,N'*-methylenediacrylamide, *N,N'*-phenylenediacrylamide, 3,5-bis(acryloylamido) benzoic acid, pentaerythritol triacrylate, trimethylolpropane trimethacrylate, pentaerytrithol tetraacrylate, trimethylolpropane ethoxylate (14/3 EO/OH) triacrylate, trimethylolpropane ethoxylate (7/3 EO/OH) triacrylate, trimethylolpropane propoxylate (1 PO/OH) triacrylate, trimethylolpropane propoxylate (2 PO/OH) triacrylate, and mixtures thereof.

75. A method according to claim 1, wherein said detecting comprises:

scanning the solid support at the particular sites and identifying if ligation of the oligonucleotide probe sets occurred and

correlating identified ligation to a presence or absence of the target nucleotide sequences.

76. A method according to claim 75, wherein said scanning is carried out by scanning electron microscopy, electron microscopy, confocal microscopy, charge-coupled

device, scanning tunneling electron microscopy, infrared microscopy, atomic force microscopy, electrical conductance, and fluorescent or phosphor imaging.

77. A method according to claim 75, wherein said correlating is carried out with a computer.

78. A method according to claim 1, wherein said contacting the mixture with the solid support is at a temperature of 45-90°C and for a time period of up to 60 minutes.

79. A method according to claim 1, wherein some of the plurality of capture oligonucleotides have identical nucleotide sequences and different labels are used for some different target nucleotide sequence.

80. A method according to claim 1, wherein the plurality of capture oligonucleotides each have different nucleotide sequences.

81. A method according to claim 80, wherein each capture oligonucleotide differs from its adjacent capture oligonucleotide on the array by at least 25% of the nucleotides.

82. A method according to claim 80, wherein each capture oligonucleotide has adjacent capture oligonucleotides separated from adjacent capture oligonucleotides by barrier oligonucleotides to which ligated oligonucleotide probe sets will not hybridize during said contacting.

83. A method according to claim 1, wherein the oligonucleotide probe sets hybridize to the target nucleotide sequences at temperatures which are less than that at which the capture oligonucleotides hybridize to the addressable array-specific portion of oligonucleotide probe sets.

84. A method according to claim 1 further comprising:

treating the mixture chemically or enzymatically, after said subjecting the mixture to a series of ligase detection reaction cycles, to destroy unligated oligonucleotide probes.

85. A method according to claim 84, wherein said treating is carried out with an exonuclease.

86. A method according to claim 1 further comprising:

removing oligonucleotides bound to the capture oligonucleotides to permit reuse of the solid support with immobilized capture oligonucleotides.

87. A method according to claim 1, wherein the solid support includes different capture oligonucleotides immobilized at different sites with different capture oligonucleotides being complementary to different addressable array-specific portions, whereby different oligonucleotide probe sets are captured and detected at different sites on the solid support.

88. A method according to claim 1, wherein the solid support includes identical capture oligonucleotides immobilized on the solid support with the capture oligonucleotides being complementary to all the addressable array-specific portions and the labels attached to the oligonucleotide probe sets being different, whereby the different oligonucleotide probe sets are detected and distinguished by the different labels.

89. A method of forming arrays of oligonucleotides on a solid support comprising:

providing a solid support having an array of positions each suitable for attachment of an oligonucleotide;

attaching to the solid support a surface or linker, suitable for coupling an oligonucleotide to the solid support, at each of the array positions; and

forming the array of a plurality of capture oligonucleotides on the solid support by a series of cycles of activating selected array positions for attachment of multimer nucleotides and attaching multimer nucleotides at the activated array positions.

90. A method according to claim 89, wherein said forming comprises:

applying a multimer nucleotide along parallel rows of the solid support;

turning the support 90 degrees;

attaching a multimer nucleotide along parallel rows of the solid support to form oligonucleotides at row intersections having 2 sets of multimer nucleotides; and

repeating said applying, turning, and attaching until the oligonucleotides at the row intersections have 6 sets of multimer nucleotides.

91. A method according to claim 89, wherein the solid support is made from a material selected from the group consisting of plastic, ceramic, metal, resin, gel, glass, silicon, and composites thereof.

92. A method according to claim 89, wherein the solid support is in a form selected from the group consisting of slides, discs, membranes, films, and composites thereof.

93. A method according to claim 89, wherein the solid support has an array of positions with the plurality of capture oligonucleotides having different nucleotide sequences.

94. A method according to claim 93, wherein the solid support has wells, raised regions, or etched trenches.

95. A method according to claim 94, wherein the solid support is in the form of a microtiter plate.

96. A method according to claim 89, wherein said attaching a linker comprises: silanizing a surface of the solid support.

97. A method according to claim 89, wherein the solid support is functionalized with olefin, amino, hydroxyl, silanol, aldehyde, keto, halo, acyl halide, or carboxyl groups.

98. A method according to claim 97, wherein the solid support is functionalized with an amino group by reaction with an amine compound selected from the group consisting of 3-aminopropyl triethoxysilane, 3-aminopropylmethyldiethoxysilane, 3-aminopropyl dimethylethoxysilane, 3-aminopropyl trimethoxysilane, N-(2-aminoethyl)-3-aminopropylmethyl dimethoxysilane, N-(2-aminoethyl-3-aminopropyl) trimethoxysilane, aminophenyl trimethoxysilane, 4-aminobutyldimethyl methoxysilane, 4-aminobutyl triethoxysilane, aminoethylaminomethylphenethyl trimethoxysilane, and mixtures thereof.

99. A method according to claim 97, wherein the solid support is functionalized with an olefin-containing silane.

100. A method according to claim 99, wherein the olefin-containing silane is selected from the group consisting of 3-(trimethoxysilyl)propyl methacrylate, *N*-[3-(trimethoxysilyl)propyl]-*N'*-(4-vinylbenzyl)ethylenediamine, triethoxyvinylsilane, triethylvinylsilane, vinyltrichlorosilane, vinyltrimethoxysilane, vinyltrimethylsilane, and mixtures thereof.

101. A method according to claim 99, wherein the silanized support is polymerized with an olefin containing monomer.

102. A method according to claim 101, wherein the olefin-containing monomer contains a functional group.

103. A method according to claim 102, wherein the olefin-containing monomer is selected from the group consisting of acrylic acid, methacrylic acid, vinylacetic acid, 4-vinylbenzoic acid, itaconic acid, allyl amine, allylethylamine, 4-aminostryrene, 2-aminoethyl methacrylate, acryloyl chloride, methacryloyl chloride, chlorostyrene, dichlorostyrene, 4-hydroxystyrene, hydroxymethylstyrene, vinylbenzyl alcohol, allyl alcohol, 2-hydroxyethyl methacrylate, poly(ethylene glycol) methacrylate, and mixtures thereof.

104. A method according to claim 101, wherein the support is polymerized with a monomer selected from the group consisting of acrylic acid, acrylamide, methacrylic acid, vinylacetic acid, 4-vinylbenzoic acid, itaconic acid, allyl amine, allylethylamine, 4-aminostyrene, 2-aminoethyl methacrylate, acryloyl chloride, methacryloyl chloride, chlorostyrene, dischlorostyrene, 4-hydroxystyrene, hydroxymethyl styrene, vinylbenzyl alcohol, allyl alcohol, 2-hydroxyethyl methacrylate, poly(ethylene glycol) methacrylate, and mixtures thereof, together with a monomer selected from the group consisting of acrylic acid, methacrylic acid, vinylacetic acid, 4-vinylbenzoic acid, itaconic acid, allyl amine, allylethylamine, 4-aminostyrene, 2-aminoethyl methacrylate, acryloyl chloride, methacryloyl chloride, chlorostyrene, dichlorostyrene, 4-hydroxystyrene, hydroxymethyl styrene, vinylbenzyl alcohol, allyl alcohol, 2-hydroxyethyl methacrylate, poly(ethylene glycol) methacrylate, methyl acrylate, methyl methacrylate, ethyl acrylate, ethyl methacrylate, styrene, 1-vinylimidazole, 2-vinylpyridine, 4-vinylpyridine, divinylbenzene, ethylene glycol dimethacrylate, *N,N'*-methylenediacrylamide, *N,N'*-phenylenediacrylamide, 3,5-bis(acryloylamido) benzoic acid, pentaerythritol triacrylate, trimethylolpropane trimethacrylate, pentaerytrithol tetraacrylate, trimethylolpropane ethoxylate (14/3 EO/OH) triacrylate, trimethylolpropane ethoxylate (7/3 EO/OH) triacrylate, trimethylolpropane propoxylate (1 PO/OH) triacrylate, trimethylolpropane propoxylate (2 PO/OH) triacrylate, and mixtures thereof.

105. A method according to claim 99, wherein said forming comprises:

photolithographically masking the solid support;

photochemically deprotecting the linker or outermost nucleotides attached to the solid support at unmasked array positions; and

adding nucleotides with a photoactivatable protecting group at photochemically deprotected array positions.

106. A method according to claim 105, wherein the photoactivable protecting group is selected from the group consisting of nitroveratryloxycarbonyl, o-nitrobenzyloxycarbonyl, fluorenylmethoxycarbonyl, dimethyl-dimethoxybenzyloxycarbonyl, oxymethyleneanthraquinone, and mixtures thereof.

107. A method according to claim 105, wherein the protecting group protects the nucleotides at their 3' or 5' ends.

108. A method according to claim 105 further comprising:

washing the solid support after said photochemically deprotecting and said adding.

109. A method according to claim 89, wherein the surface or linker is non-hydrolyzable.

110. A method according to claim 89, wherein the solid support has an array of positions with the plurality of capture oligonucleotides having the same nucleotide sequences.

111. A method according to claim 93, wherein each capture oligonucleotide differs from its adjacent capture oligonucleotide on the array by at least 25% of the nucleotides.

112. A method according to claim 93, wherein each capture oligonucleotide is separated from adjacent capture oligonucleotides by barrier oligonucleotides which are shorter than the capture oligonucleotides.

113. A method according to claim 89, wherein said method is carried out with a device having a plurality of chambers having separate valves on separate connections to a source of the multimer nucleotides and to a source of vacuum, said method further comprising:

orienting the device and the solid support for application of the multimer nucleotides to the solid support;

opening the valve to the source of vacuum to seal the chambers of the device against the solid support;

closing the valve to the source of vacuum;

opening the valve to the source of multimer nucleotides to supply the multimer nucleotides to the chambers for the attaching of multimer nucleotides at the activated array positions; and

closing the valve to the source of multimer nucleotides after the attaching.

114. A method according to claim 113, wherein the device has the chambers separately along rows and columns of the array.

115. A method according to claim 113, wherein the device has the chambers along rows of the array.

116. A method according to claim 115, wherein the chambers are configured to deliver multimer nucleotides a precise column positions.

117. A method according to claim 115, wherein said forming comprises:

applying a multimer nucleotide along parallel rows of the solid support;

turning the support 90 degrees;

attaching a multimer nucleotide along parallel rows of the solid support to form oligonucleotides at row intersections having 2 sets of multimer nucleotides by said opening the valve to the source of vacuum, said closing the valve to the source of vacuum, said opening the valve to the source of multimer nucleotides, and said closing the valve to the source of multimer nucleotides; and

repeating said applying, turning, and attaching until the oligonucleotides are formed at the row intersections.

118. A method according to claim 113, wherein said device comprises a valve block assembly with plural input ports leading to sources of multimer nucleotides and plural output ports leading to chambers.

119. A method according to claim 118, wherein the valve block assembly is cylindrical and has 2 adjacent rotatable portions which can be positioned relative to one another to connect selectively the input and output ports.

120. An array of oligonucleotides on a solid support comprising:

a solid support having an array of positions each suitable for attachment of an oligonucleotide;

a linker or support suitable for coupling an oligonucleotide to the solid support attached to the solid support at each of the array positions;

and an array of oligonucleotides on the solid support with at least some of the array positions being occupied by oligonucleotides having greater than sixteen nucleotides.

121. An array according to claim 120, wherein different oligonucleotides are attached at different array positions on the solid support to detect different nucleic acids.

122. An array according to claim 120, wherein the solid support is made from a material selected from the group consisting of plastic, ceramic, metal, resin, gel, glass, silicon, and composites thereof.

123. An array according to claim 120, wherein the solid support is in a form selected from the group consisting of slides, discs, membranes, films, and composites thereof.

124. An array according to claim 120, wherein the solid support has an array of positions with oligonucleotides attached to the array of positions.

125. An array according to claim 124, wherein the solid support has wells, raised regions, or etched trenches.

126. An array according to claim 125, wherein the solid support is in a microtiter plate.

127. An array according to claim 120, wherein the linker comprises a silane on a surface of the solid support.

128. An array according to claim 120, wherein the solid support is functionalized with olefin, amino, hydroxyl, silanol, aldehyde, keto, halo, acyl halide, or carboxyl groups.

129. An array according to claim 128, wherein the solid support is functionalized with an amino group by reaction with an amine compound selected from the group consisting of 3-aminopropyl triethoxysilane, 3-aminopropylmethyldiethoxysilane, 3-aminopropyl dimethylethoxysilane, 3-aminopropyl trimethoxysilane, N-(2-aminoethyl)-3-aminopropylmethyl dimethoxysilane, N-(2-aminoethyl-3-aminopropyl) trimethoxysilane, aminophenyl trimethoxysilane, 4-aminobutyldimethyl methoxysilane, 4-aminobutyl triethoxysilane, aminoethylaminomethylphenethyl trimethoxysilane, and mixtures thereof.

130. An array according to claim 128, wherein the solid support is functionalized with an olefin-containing silane.

131. An array according to claim 130, wherein the olefin-containing silane is selected from the group consisting of 3-(trimethoxysilyl)propyl methacrylate, *N*-[3-(trimethoxysilyl)propyl]-*N'*-(4-vinylbenzyl)ethylenediamine, triethoxyvinylsilane,

triethylvinylsilane, vinyltrichlorosilane, vinyltrimethoxysilane, vinyltrimethylsilane, and mixtures thereof.

132. An array according to claim 130, wherein the silanized support is polymerized with an olefin containing monomer.

133. An array according to claim 132, wherein the olefin-containing monomer contains a functional group.

134. An array according to claim 133, wherein the olefin-containing monomer is selected from the group consisting of acrylic acid, methacrylic acid, vinylacetic acid, 4-vinylbenzoic acid, itaconic acid, allyl amine, allylethylamine, 4-aminostyrene, 2-aminoethyl methacrylate, acryloyl chloride, methacryloyl chloride, chlorostyrene, dichlorostyrene, 4-hydroxystyrene, hydroxymethylstyrene, vinylbenzyl alcohol, allyl alcohol, 2-hydroxyethyl methacrylate, poly(ethylene glycol) methacrylate, and mixtures thereof.

135. An array according to claim 132, wherein the support is polymerized with a monomer selected from the group consisting of acrylic acid, acrylamide, methacrylic acid, vinylacetic acid, 4-vinylbenzoic acid, itaconic acid, allyl amine, allylethylamine, 4-aminostyrene, 2-aminoethyl methacrylate, acryloyl chloride, methacryloyl chloride, chlorostyrene, dichlorostyrene, 4-hydroxystyrene, hydroxymethyl styrene, vinylbenzyl alcohol, allyl alcohol, 2-hydroxyethyl methacrylate, poly(ethylene glycol) methacrylate, and mixtures thereof, together with a monomer selected from the group consisting of acrylic acid, methacrylic acid, vinylacetic acid, 4-vinylbenzoic acid, itaconic acid, allyl amine, allylethylamine, 4-aminostyrene, 2-aminoethyl methacrylate, acryloyl chloride, methacryloyl chloride, chlorostyrene, dichlorostyrene, 4-hydroxystyrene, hydroxymethyl styrene, vinylbenzyl alcohol, allyl alcohol, 2-hydroxyethyl methacrylate, poly(ethylene glycol) methacrylate, methyl acrylate, methyl methacrylate, ethyl acrylate, ethyl methacrylate, styrene, 1-vinylimidazole, 2-vinylpyridine, 4-vinylpyridine, divinylbenzene, ethylene glycol dimethacrylate, *N,N'*-methylenediacrylamide, *N,N'*-phenylenediacrylamide, 3,5-bis(acryloylamido) benzoic acid, pentaerythritol triacrylate, trimethylolpropane trimethacrylate, pentaerytrithol tetraacrylate, trimethylolpropane ethoxylate (14/3 EO/OH) triacrylate, trimethylolpropane ethoxylate (7/3 EO/OH) triacrylate, trimethylolpropane propoxylate (1 PO/OH) triacrylate, trimethylolpropane propoxylate (2 PO/OH) triacrylate, and mixtures thereof.

136. An array according to claim 120, wherein the linker or support is non-hydrolyzable.

137. An array according to claim 120, wherein the array is reusable for repeatedly hybridizing oligonucleotides to the array of oligonucleotides on the solid support.

138. A kit for identifying one or more of a plurality of sequences differing by single-base changes, insertions, deletions, or translocations in a plurality of target nucleotide sequences comprising:

a ligase;

a plurality oligonucleotide probe sets, each characterized by (a) a first oligonucleotide probe, having a target sequence-specific portion and an addressable array-specific portion, and (b) a second oligonucleotide probe, having a target sequence-specific portion and detectable reporter label, wherein the oligonucleotide probes in a particular set are suitable for ligation together when hybrided adjacent to one another on a respective target nucleotide sequence, but have a mismatch which interferes with such ligation when hybridized to any other nucleotide sequence, present in the sample; and

a solid support with capture oligonucleotides immobilized at particular sites, wherein the capture oligonucleotides have nucleotide sequences complementary to the addressable array-specific portions.

139. A kit according to claim 138, wherein the mismatch of oligonucleotide probe sets to nucleotide sequences other than their respective target nucleotide sequences is at a base at a ligation junction at which the oligonucleotide probe of each set ligate together when hybridized to their respective target nucleotide sequences.

140. A kit according to claim 138, wherein the mismatch is on the oligonucleotide probe of the oligonucleotide probe sets which have 3' ends at the ligation junction.

141. A kit according to claim 138, wherein the mismatch of oligonucleotide probe sets to nucleotide sequences other than their respective target nucleotide sequence is at a base adjacent to a ligation junction at which the oligonucleotide probes of each set ligate together when hybridized to their respective target nucleotide sequences.

142. A kit according to claim 141, wherein the mismatch is on the oligonucleotide probe of the oligonucleotide probe sets which have 3' ends at the ligation junction.

143. A kit according to claim 138, wherein the ligase is selected from the group consisting of *Thermus aquaticus* ligase, *Thermus thermophilus* ligase, *E. coli* ligase, T4 ligase, and *Pyrococcus* ligase.

144. A kit according to claim 138 further comprising:

amplification primers suitable for preliminary amplification of the target nucleotide sequences and

a polymerase.

145. A kit according to claim 138, wherein the solid support includes different capture oligonucleotides immobilized at different particular sites with different capture oligonucleotides being complementary to different addressable array-specific portions, whereby different oligonucleotide probe sets are hybridized and detected at different sites on the solid support.

146. A kit according to claim 138, wherein the solid support includes identical capture oligonucleotides immobilized on the solid support with the capture oligonucleotides complementary to all the addressable array-specific portions and the labels attached to the oligonucleotide probe sets being different, whereby the oligonucleotide probe sets are detected and distinguished by the different labels.

147. A kit according to claim 138, wherein the oligonucleotide probe sets and the capture oligonucleotides are configured so that the oligonucleotide probe sets hybridize, respectively, to the target nucleotide sequences at temperatures which are less than that at which the capture oligonucleotides hybridize to the addressable array-specific portions of the oligonucleotide probes sets.